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10/682,271	10/09/2003	Jeffrey W. Leon	86363LMB	8270

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

PTOL-90A (Rev. 04/07)

Office Action Summary	Application No.	Applicant(s)	
	10/682,271	LEON ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *2-11,13-33 and 37-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12 and 34-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 March 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group X, Claims 1,12 and 34-36 is acknowledged. The traversal is on the ground(s) that a design is not materially different just because the support may be made of two different materials. The biological microarrays of the claims all have the same design, function and effect. Furthermore, the inventions as claimed encompass overlapping subject matter, as they all relate to a biological microarray of filler, functional compound and gelatin. One of ordinary skill in the art would consider supports of glass and plastic from Groups I and II to be obvious variants. One of ordinary skill in the art would consider the fillers from Groups III- X to be obvious variants. One of ordinary skill in the art would consider functional compounds of Groups XI-XIV, based on claim 43, to be obvious variants. In addition, claim 1 requires the functional compound to be compatible with a biological capture agent, making the inclusion of a biological capture agent from Group XV to be an obvious variant. The Examiner's own analysis indicates that all of the Invention Groups identified are contained in a single class, class 436. The Examiner has also indicated that the Invention Groups only relate to 4 subclasses, sub-classes 527, 531, 518+ and 524. Thus, coextensive searching of the Groups would not prove seriously burdensome to the Examiner, but would instead be most efficient. This is not found persuasive because as apparent from applicants' traversal above, each of the groups, differ in one or more components albeit all are drawn to microarray, as argued. Thus, examination of each and every component in a microarray, contained in one group, but not in the other groups, would entail undue burden of examination i.e., to examine each and every different species of the genus claims. The search is not limited to US Patents but also to other commercial databases and foreign Patents. Thus, while the search for the patents might be co-extensive however, the search of commercial databases is not co-extensive with the US and foreign Patents.

The requirement is still deemed proper and is therefore made FINAL.

Applicants' election of the species, colloidal silica is noted. The species election is made without traverse.

Claims 2-11, 13-33 and 37-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement made on 3/30/07.

Status of Claims

Claims 1-69 are pending.

Claims 2-11, 13-33 and 37-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1, 12 and 34-36 are under consideration.

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 12 and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is unclear whether the one layer comprises as a single entity the filler and gelatin coating the support or the support is coated with gelatin to which is added filler and the functional groups are overlayed. The term "reducing" in claim 1 is a relative term which renders the claim indefinite. This term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear as to the basis, measure or extent of the filler and gelatin reduction of fluorescence especially in the absence of recitation of a specific filler component.

2. Claims 35 and 36 are grammatically incorrect.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 12 and 34-36 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6815078 ('078 Patent) or claim 1 of U.S. Patent No. 6797393 ('393 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant broad term "support" includes the '078 Patent "polymer scaffold". Likewise the '393 Patent, which recites a trifunctional group includes the instant bifunctional group. The bifunctional group with a linker is obviously a trifunctional group.

Claim Rejections - 35 USC § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 12 and 34-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al(USP 7179638).

Anderson et al discloses at claim 6:

> A microarray comprising a solid phase support and at least about 500 cells per square centimeter wherein each cell contains an agent of interest that is not chemically bound to the solid phase support and a plurality of structures (filler and gelatin) bound to said solid phase support, wherein each of a plurality of structures has an immobilized agent of interest(functional groups, as claimed) available for binding to a target, wherein the target is a binding partner for the agent of interest, and wherein the microarray contains a plurality of different agents of interest in a corresponding plurality of different structures, wherein each of the structure forms a hollow chamber with the agent of interest immobilized on an inner surface of the hollow chamber.

Anderson discloses the various components comprised in the microarray at e.g., col. 5, line 60 up to col. 11, line 37

> In a still further aspect, the invention relates to the incorporation of a non-fluorescent dye or other light absorbing material in the substance of the array to control the depth to which light used to excite fluorescence penetrates the array, thereby controlling the depth to which fluorescence analytes are detected, and insuring that fluorescent analytes which diffuse too deeply into the content of the cells, and therefore do not diffuse out, are not detected.

The term "particle" includes a large number of insoluble materials of any configuration, including spherical, thread-like, brush-like and many irregular shapes. Particles are frequently porous with regular or random channels inside. Examples include silica, cellulose, Sepharose beads, polystyrene (solid, porous and derivitized) beads, controlled-pore glass, gel beads, sols, biological cells, subcellular particles, microorganisms (protozoans, bacteria, yeast, viruses, etc.) micelles, liposomes, cyclodextrins, two phase systems (e.g. agarose beads in wax) etc. and other structures which entrap or encapsulate a material. Particularly preferred are recombinant hosts and viruses that express the protein of interest. Even certain high molecular weight materials, such as, polymers and complexes, may serve as immobilizing structures that would constitute a "particle".

The terms "arrays" and "microarrays" are used somewhat interchangeably differing only in general size. The instant invention involves the same methods for making and using either. Each array typically contains many cells (typically 100 1,000,000+) wherein each cell is at a known location and contains a specific component of interest. Each array therefore contains numerous different components of interest.

In a related aspect, "device" is used to describe both arrays and microarrays, where the array or microarray may comprise other defined components including surfaces and points of contact between reagents.

Further, "substrate" is also a term used to describe surfaces as well as solid phases which may comprise the array, microarray or device.

A fifth class of fibers is comprised of hollow impermeable tubules typically formed from plastics including, but not limited to, polyethylene, polypropylene, Teflon.RTM. or polyvinyl chloride, and is filled completely with a gel or other polymerizing material to which agents of interest are

> attached directly. The external surfaces of the tubes may be modified chemically or physically to accept adhesives used to bind the bundled tubes together. The internal surface also may be modified so that the gel or polymerizing mixture introduced into the tubes will adhere, preferably by covalent attachment. Acrylamide derivatives may be linked to the wall to make an acrylamide gel adhere, while ***gelatin,*** agar, or agarose derivatives may be attached similarly to link with the respective gels. Methods for linking agents of interest, such as, proteins and nucleic acids, to linear acrylamide, ***gelatin*** and agarose are well known, and the derivatized molecules can be incorporated into the gels used for casting. Acrylamide can be made to gel at room temperature either chemically or using photoactivation, while low temperature-gelling Sepharose is available. ***Gelatin*** sets slowly and at temperatures below ambient. The polymers used to fill the tubes are typically homogeneous, but may contain agents of interest, which become attached to the polymerizing medium. Examples include covalent attachment of proteins to short acrylamide chains that become incorporated into acrylamide gels and proteins covalently linked to ***gelatin***. Thus, gels are available or can be produced which contain labile biomolecules without exposing them to denaturing temperatures. The structure of such tubes is illustrated in FIG. 3 where tube 16 is filled with a cross-linked gel 17 to which are attached agents of interest 18. A side view 19 and end view 21 of a sectioned tube illustrates the availability of immobilized agents 21.

Accordingly, the claimed biological microarray comprising of the broad claimed components are fully met by the biological microarray of Anderson, which discloses all the claimed elements of the claimed biological microarray.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 12, 34 and 36 are rejected under 35 U.S.C. 103(a) as being obvious over Qiao et al(USP 6797393('393 Patent) or 6815078('078 Patent)).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130

stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Qiao et al ('393 Patent disclose e.g., at the abstract a gelatin-based substrate for fabricating protein arrays, the substrate containing: gelatin and a trifunctional compound A--L--B; wherein A is a functional group capable of interacting with the gelatin; L is a linking group capable of interacting with A and with B; and B is a functional group capable of interacting with a protein capture agent. A may be the same or different from B.

It would have been obvious that the instant functional groups (first and second) contains a linker to enable linking one group to the gelatin coated substrate and the other to a capture agent. Thus, the instant broad functional groups encompass the trifunctional groups which recite a linker, linking the two functional groups.

Qiao et al('078 Patent) disclose at the abstract, for example, a gelatin-based substrate for fabricating protein arrays, the substrate comprising: gelatin having at least one surface; a polymer scaffold affixed to the gelatin surface; wherein the polymer in the scaffold is rich in reactive units capable of immobilizing proteins.

See the obviousness double patenting rejection above.

Claims 1, 12, 34 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Murphy (USP 7018838) or Marchina et al(Int. J. Biochem. Cell Biol.) in view of Arenkov (Anal. Biochemistry).

Murphy discloses a biological microarray as used in the method at the SUMMARY of INVENTION e.g., col.9, lines 48-67:

> Methods for culturing cells comprising: providing a liquid crystal substrate (filler microarray, as claimed) and cells (functional groups, as claimed); and culturing the cells on the liquid crystal substrate. The present invention is not limited to the use of any particular types of liquid crystals. Indeed, the use of a variety of liquid crystal types is contemplated, including, but not limited to, lyotropic liquid crystals and thermotropic liquid crystals. In some embodiments, the liquid crystal substrate comprises a matrix. The present invention is not limited to any particular type of matrix. Indeed, the use of a variety of matrices is contemplated, including, but not limited to, extracellular matrices such as reconstituted basement membrane like complexes such as derived from some eukaryotic cell lines (e.g., EHS cells), collagen, fibronectin, laminin, vitronectin and ***gelatin,*** a bacterial

> extracellular matrix, a gel matrix, and polymeric matrices. In still other embodiments, the liquid crystal substrate comprises a moiety selected from the group consisting of phospholipids and biological receptors.

Thus, Murphy discloses in the above assay a biological microarray comprising of a gelatin contained in the liquid crystal (which can read on the claimed filler).

Murphy discloses at the DEFINITIONS section at e.g., col. 14, line 36:

> The term "substrate" refers to material capable of supporting associated assay components (e.g., assay regions, mesogens that constitute the functional units of liquid crystals, cells, test compounds, etc.). For example, in some embodiments, the substrate comprises a planar (i.e., 2 dimensional) glass, metal, composite, plastic, ***silica,*** or other biocompatible or biologically unreactive (or biologically reactive) composition. In some other embodiments, the substrate comprises a porous (e.g., microporous) or structured (i.e., 3 dimensional) composition (e.g., sol-gel matrices).
>
> As used herein, "array" refers to a substrate with a plurality of molecules (e.g., mesogens, recognition moieties) and/or structures (e.g., wells, reservoirs, channels, and the like) associated with its surface in an orderly arrangement (e.g., a plurality of rows and columns). In another sense, the term "array" refers to the orderly arrangement (e.g., rows and columns) of two or more assay regions on a substrate.
>
> The term "nanostructures" refers to microscopic structures, typically measured on a nanometer scale. Such structures include various three-dimensional assemblies, including, but not limited to, liposomes, films, multilayers, braided, lamellar, helical, tubular, pillar like and fiber-like shapes, and combinations thereof.

> As used the term "multilayer" refers to structures comprised of two or more monolayers. The individual monolayers may chemically interact with one another to produce a film with novel properties (i.e., properties that are different from those of the monolayers alone).

Marchina et al discloses at page 1143, col. 2 a fibronectin molecule immobilized onto round glass coverslips placed in 24-well multidishes previously treated with gelatin.

Murphy or Marchina does not disclose a fluorescence reducing filler, as claimed.

Arenkov discloses at page 125, col. 2 (REUSLTS section):

> A gel support polyacrylamide gel provides a stable, low-fluorescence background, low nonspecific absorption, high-capacity support for immobilization of different compounds on microchips. However, the rather low porosity of conventional polyacrylamide gels retards diffusion into the gel of the macromolecules that interact with the immobilized compounds. More porous gels can be prepared by increasing the ratio of the crosslinker Bis to acrylamide from 1:19 to 1:3 (10). The use of N,N'-diallyltartardiamide (DATD) as a crosslinker also improves the porosity of the microchip gels (6); however, DATD inhibits polymerization of acrylamide-based gels (10). Here, a further increase in porosity was achieved by the use of N,N'-(1,2-dihydroxyethylene)bisacrylamide (DHEBA)-Bis mixture (10, 11) instead of DATD as a crosslinker and partial splitting of the crosslinking DHEBA molecules by oxidation of their vicinal dihydroxy groups with NaIO4. The high porosity of this gel and easy access of macromolecules inside the gel pads enabled us to regulate the amount of immobilized compounds and thus the sensitivity of measurements by variations in the size of the microchip elements. The change in thickness of the 100 × 100-/xm gel pads from 20 to 40/zm increased the amount of immobilized antibodies(first functional group as claimed) and enhanced the fluorescence signals for antigen(second functional group, as broadly claimed) detection by about twofold.

Accordingly, it would have been obvious to one having ordinary skill in the art to include a stable, low-fluorescence compound as polyacrylamide gel in the biological microarray of Murphy or Marchina as taught by Arenkov. The motivation would have been obvious to one having ordinary skill in the art i.e., to reduce fluorescence of high~~-~~fluorescent background compounds, as ~~gelatin.~~

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy or Marchina in view of Arenkov as applied to claims 1, 12, 34 and 36 above, and further in view of Chari (USP 6649312).

Murphy or Marchina does not disclose a colloidal silica in the biological array. Chari discloses at e.g., col. 11, line 53 up to col. 12, line 61:

> The quantities of the various ingredients and their relationship to each other in the polymer suspension process can vary over wide ranges, however, it has generally been found that the ratio of the polymer to the solvent should vary in an amount of from about 1 to about 80% by weight of the combined weight of the polymer and the solvent and that the combined weight of the polymer and the solvent should vary with respect to the quantity of water employed in an amount of from about 25 to about 50% by weight. The size and quantity of the colloidal silica stabilizer depends upon the size of the particles of the colloidal silica and also upon the size of the polymer droplet particles desired. Thus, as the size of the polymer/solvent droplets are made smaller by high shear agitation, the quantity of solid colloidal stabilizer is varied to prevent uncontrolled coalescence of the droplets and to achieve uniform size and narrow size distribution of the polymer particles that result. These techniques provide particles having a predetermined average diameter anywhere within the range of from 0.5 micrometer to about 150 micrometers with a very narrow size distribution. The coefficient of variation (ratio of the standard deviation to the average diameter, as described in U.S. Pat. No. 2,932,629) is normally in the range of about 15 to 35%.

Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to include a colloidal silica in biological array components of Murphy or Marchina since said colloidal stabilizes the polymer as taught by Chari. This advantage would motivate one having ordinary skill in the art to incorporate a colloidal stabilizer to a microarray.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The xaminer can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0765. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T.D.
T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
April 27, 2007